

# Karyopharm Announces FDA Approval of XPOVIO® (selinexor) for the Treatment of Patients with Relapsed or Refractory Diffuse Large B-cell Lymphoma (DLBCL)

**-- XPOVIO is Now the Only Single-Agent, Oral Therapy Approved for the Treatment of Patients with Relapsed or Refractory Diffuse Large B-cell Lymphoma, Including DLBCL Arising from Follicular Lymphoma --**

**-- XPOVIO is the First and Only FDA-Approved Drug for Use in Both Multiple Myeloma and DLBCL --**

**-- Conference Call Scheduled for Today at 12:30 p.m. Eastern Time --**

NEWTON, Mass., June 22, 2020 (GLOBE NEWSWIRE) -- Karyopharm Therapeutics Inc. (Nasdaq:KPTI), an innovation-driven pharmaceutical company, today announced that the U.S. Food and Drug Administration (FDA) has approved oral XPOVIO® (selinexor), the Company's first-in-class, Selective Inhibitor of Nuclear Export (SINE) compound, for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified, including DLBCL arising from follicular lymphoma, after at least two lines of systemic therapy. This indication was approved based on response rate under the FDA's Accelerated Approval Program, which was developed to allow for expedited approval of drugs that treat serious conditions and that fill an unmet medical need. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

XPOVIO will be commercially available immediately in this new indication in the U.S. and Karyopharm will leverage its existing commercial infrastructure to market this second oncology indication. A Marketing Authorization Application for selinexor for relapsed or refractory DLBCL is planned for submission to the European Medicines Agency in 2021.

"The accelerated approval of oral XPOVIO in patients with relapsed or refractory DLBCL is a significant milestone for the patients and families who currently have limited treatment options available for their disease," said Sharon Shacham, PhD, MBA, Founder, President and Chief Scientific Officer of Karyopharm. "This approval marks the first for an oral agent for patients with previously treated DLBCL and the first approval of any single drug for this highly aggressive type of lymphoma. Additionally, this is now the second commercial oncology indication for XPOVIO, highlighting its novel mechanism of action, ease of administration and ability to produce rapid and durable responses in patients with heavily pretreated disease. We share this tremendous achievement with the patients, employees, caregivers and physicians who have tirelessly contributed to the advancement of XPOVIO from its original discovery and clinical development to today's second FDA approval."

"For the significant number of patients with relapsed or refractory DLBCL, there is an important need for new therapies for this particularly vulnerable patient population. Unfortunately, despite often multiple types of chemotherapy and targeted-drug combination therapy, many patients have disease which continues to progress," said John P. Leonard, MD, the Richard T. Silver Distinguished Professor of Hematology and Medical Oncology at Weill Cornell Medicine and an oncologist at NewYork-Presbyterian/Weill Cornell Medical Center.<sup>1</sup> "Single agent, oral XPOVIO demonstrated a clinically meaningful overall response rate of 29%, including a complete response rate of 13%, in the pivotal SADAL study across several disease subtypes. Importantly, some patient responses were durable with 38% of responding patients maintaining a response at 6 months. The clinical profile and tolerability of oral XPOVIO provides physicians and patients with a new treatment alternative to traditional intravenous chemotherapy regimens."

"We will initiate our XPOVIO commercial launch efforts in DLBCL immediately, expanding our reach across the country for cancer patients in need," said Michael G. Kauffman, MD, PhD, Chief Executive Officer of Karyopharm. "Since our founding in 2008, Karyopharm has been focused on exploring the potential of nuclear transport modulators and we are thrilled to now enter this new chapter of growth with our dual-commercialization of the first and only nuclear export inhibitor approved in the U.S."

## About the Phase 2b SADAL Study

The accelerated FDA approval of XPOVIO is based on the results from the multi-center, single-arm Phase 2b SADAL (Selinexor Against Diffuse Aggressive Lymphoma) study (NCT02227251), which evaluated 134 patients (median of 2 prior systemic therapies with a range of 1-5) with relapsed or refractory DLBCL. Patients were administered a fixed 60 mg dose of XPOVIO given orally twice weekly for a four-week cycle. Patients with

germinal center B-cell (GCB) or non-GCB subtypes of DLBCL were included in enrollment.

The SADAL study met its primary endpoint of overall response rate (ORR) with an ORR of 29%, including 18 (13%) complete responses (CRs) and 21 (16%) partial responses (PRs).

Key secondary endpoints included a median duration of response (DOR) in the responding patients. In the responding patients, 56% maintained a response at 3 months, 38% at 6 months and 15% at 12 months.

All 134 patients were included in the safety analyses. The most common treatment-related adverse events (AEs) were cytopenias along with gastrointestinal and constitutional symptoms and were generally reversible and managed with dose modifications and/or standard supportive care. The most common non-hematologic AEs were fatigue (63%), nausea (57%), decreased appetite (37%), and diarrhea (37%), and were mostly Grade 1 and 2 events. Grade 3 and 4 laboratory abnormalities in  $\geq 15\%$  of patients included thrombocytopenia, lymphopenia, neutropenia, anemia, and hyponatremia. Grade 4 laboratory abnormalities in  $\geq 5\%$  of patients were thrombocytopenia (18%), lymphopenia (5%), and neutropenia (9%).

As part of the FDA accelerated approval, the FDA has agreed that the XPORT-DLBCL-030 study could serve as the confirmatory trial for evaluating selinexor in DLBCL. This trial will assess the effect of selinexor or placebo added to a standard backbone immunochemotherapy of rituximab-gemcitabine-dexamethasone-platinum (R-GDP) in patients with 1-3 prior treatments for DLBCL. The rationale for this study is based on data from the ongoing Phase 1B study being conducted by the French Lymphoma Academic Research Organization (LYSARC) (NCT02741388). Karyopharm anticipates the XPORT-DLBCL-030 study will begin by the end of 2020.

#### Conference Call Information

Karyopharm will host a conference call today, Monday, June 22, 2020, at 12:30 p.m. Eastern Time, to discuss the FDA's approval of XPOVIO for the treatment of patients with relapsed or refractory DLBCL. To access the conference call, please dial (855) 437-4406 (local) or (484) 756-4292 (international) at least 10 minutes prior to the start time and refer to conference ID 8794658. A live audio webcast of the call will be available under "Events & Presentations" in the Investor section of the Company's website, <http://investors.karyopharm.com/events-presentations>. An archived webcast will be available on the Company's website approximately two hours after the event.

#### About XPOVIO® (selinexor)

XPOVIO is a first-in-class, oral Selective Inhibitor of Nuclear Export (SINE) compound. XPOVIO functions by selectively binding to and inhibiting the nuclear export protein exportin 1 (XPO1, also called CRM1). XPOVIO blocks the nuclear export of tumor suppressor, growth regulatory and anti-inflammatory proteins, leading to accumulation of these proteins in the nucleus and enhancing their anti-cancer activity in the cell. The forced nuclear retention of these proteins can counteract a multitude of the oncogenic pathways that, unchecked, allow cancer cells with severe DNA damage to continue to grow and divide in an unrestrained fashion. Karyopharm received accelerated U.S. Food and Drug Administration (FDA) approval of XPOVIO in July 2019 in combination with dexamethasone for the treatment of adult patients with relapsed refractory multiple myeloma (RRMM) who have received at least four prior therapies and whose disease is refractory to at least two proteasome inhibitors, at least two immunomodulatory agents, and an anti-CD38 monoclonal antibody. Karyopharm has also submitted a Marketing Authorization Application (MAA) to the European Medicines Agency (EMA) with a request for conditional approval of selinexor in this same RRMM indication. Karyopharm submitted a supplemental New Drug Application (sNDA) to the FDA requesting an expansion of its current indication to include the treatment for patients with multiple myeloma after at least one prior line of therapy based on the positive results from the Phase 3 BOSTON study which evaluated selinexor in combination with Velcade® (bortezomib) and low-dose dexamethasone. In June 2020, Karyopharm received accelerated FDA approval of XPOVIO for its second indication in adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified, including DLBCL arising from follicular lymphoma, after at least 2 lines of systemic therapy. Selinexor is also being evaluated in several other mid-and later-phase clinical trials across multiple cancer indications, including as a potential backbone therapy in combination with approved myeloma therapies (STOMP), in liposarcoma (SEAL) and in endometrial cancer (SIENDO), among others. Additional Phase 1, Phase 2 and Phase 3 studies are ongoing or currently planned, including multiple studies in combination with approved therapies in a variety of tumor types to further inform Karyopharm's clinical development priorities for selinexor. Additional clinical trial information for selinexor is available at [www.clinicaltrials.gov](http://www.clinicaltrials.gov).

For more information about Karyopharm's products or clinical trials, please contact the Medical Information department at:

Tel: +1 (888) 209-9326

Email: [medicalinformation@karyopharm.com](mailto:medicalinformation@karyopharm.com)

## IMPORTANT SAFETY INFORMATION

**Thrombocytopenia:** XPOVIO can cause life-threatening thrombocytopenia, potentially leading to hemorrhage. Thrombocytopenia was reported in patients with multiple myeloma (MM) and developed or worsened in patients with DLBCL.

Thrombocytopenia is the leading cause of dosage modifications. Monitor platelet counts at baseline and throughout treatment. Monitor more frequently during the first 3 months of treatment. Institute platelet transfusion and/or other treatments as clinically indicated. Monitor patients for signs and symptoms of bleeding and evaluate promptly. Interrupt, reduce dose, or permanently discontinue based on severity of adverse reaction.

**Neutropenia:** XPOVIO can cause life-threatening neutropenia, potentially increasing the risk of infection. Neutropenia and febrile neutropenia occurred in patients with MM and in patients with DLBCL.

Obtain white blood cell counts with differential at baseline and throughout treatment. Monitor more frequently during the first 3 months of treatment. Monitor patients for signs and symptoms of concomitant infection and evaluate promptly. Consider supportive measures, including antimicrobials and growth factors (e.g., G-CSF). Interrupt, reduce dose, or permanently discontinue based on severity of adverse reaction (AR).

**Gastrointestinal Toxicity:** XPOVIO can cause severe gastrointestinal toxicities in patients with MM and DLBCL.

**Nausea/Vomiting:** Provide prophylactic antiemetics. Administer 5-HT<sub>3</sub> receptor antagonists and other anti-nausea agents prior to and during treatment with XPOVIO. Interrupt, reduce dose, or permanently discontinue based on severity of ARs. Administer intravenous fluids to prevent dehydration and replace electrolytes as clinically indicated.

**Diarrhea:** Interrupt, reduce dose, or permanently discontinue based on severity of ARs. Provide standard anti-diarrheal agents, administer intravenous fluids to prevent dehydration, and replace electrolytes as clinically indicated.

**Anorexia/Weight Loss:** Monitor weight, nutritional status, and volume status at baseline and throughout treatment. Monitor more frequently during the first 3 months of treatment. Interrupt, reduce dose, or permanently discontinue based on severity of ARs. Provide nutritional support, fluids, and electrolyte repletion as clinically indicated.

**Hyponatremia:** XPOVIO can cause severe or life-threatening hyponatremia. Hyponatremia developed in patients with MM and in patients with DLBCL.

Monitor sodium level at baseline and throughout treatment. Monitor more frequently during the first 2 months of treatment. Correct sodium levels for concurrent hyperglycemia (serum glucose >150 mg/dL) and high serum paraprotein levels. Assess hydration status and manage hyponatremia per clinical guidelines, including intravenous saline and/or salt tablets as appropriate and dietary review. Interrupt, reduce dose, or permanently discontinue based on severity of the AR.

**Serious Infection:** XPOVIO can cause serious and fatal infections. Most infections were not associated with Grade 3 or higher neutropenia. Atypical infections reported after taking XPOVIO include, but are not limited to, fungal pneumonia and herpesvirus infection.

Monitor for signs and symptoms of infection, and evaluate and treat promptly.

**Neurological Toxicity:** XPOVIO can cause life-threatening neurological toxicities.

Coadministration of XPOVIO with other products that cause dizziness or mental status changes may increase the risk of neurological toxicity.

Advise patients to refrain from driving and engaging in hazardous occupations or activities, such as operating heavy or potentially dangerous machinery, until the neurological toxicity fully resolves. Optimize hydration status, hemoglobin level, and concomitant medications to avoid exacerbating dizziness or mental status changes. Institute fall precautions as appropriate.

**Embryo-Fetal Toxicity:** XPOVIO can cause fetal harm when administered to a pregnant woman.

Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential and males with a female partner of reproductive potential to use effective contraception during treatment with XPOVIO and for 1 week after the last dose.

## ADVERSE REACTIONS

The most common adverse reactions (ARs) in  $\geq 20\%$  of patients with MM are thrombocytopenia, fatigue, nausea, anemia, decreased appetite, decreased weight, diarrhea, vomiting, hyponatremia, neutropenia, leukopenia, constipation, dyspnea, and upper respiratory tract infection.

The most common ARs, excluding laboratory abnormalities, in  $\geq 20\%$  of patients with DLBCL are fatigue, nausea, diarrhea, appetite decrease, weight decrease, constipation, vomiting, and pyrexia. Grade 3-4 laboratory abnormalities in  $\geq 15\%$  of patients included thrombocytopenia, lymphopenia, neutropenia, anemia, and hyponatremia. Grade 4 laboratory abnormalities in  $\geq 5\%$  were thrombocytopenia, lymphopenia, and neutropenia.

In patients with MM, fatal ARs occurred in 9% of patients. Serious ARs occurred in 58% of patients. Treatment discontinuation rate due to ARs was 27%. The most frequent ARs requiring permanent discontinuation in  $\geq 4\%$  of patients included fatigue, nausea, and thrombocytopenia.

In patients with DLBCL, fatal ARs occurred in 3.7% of patients within 30 days, and 5% of patients within 60 days of last treatment; the most frequent fatal AR was infection (4.5% of patients). Serious ARs occurred in 46% of patients; the most frequent serious AR was infection. Discontinuation due to ARs occurred in 17% of patients.

## USE IN SPECIFIC POPULATIONS

In MM, no overall difference in effectiveness of XPOVIO was observed in patients  $> 65$  years old when compared with younger patients. Patients  $\geq 75$  years old had a higher incidence of discontinuation due to an AR than younger patients, a higher incidence of serious ARs, and a higher incidence of fatal ARs.

Clinical studies in patients with relapsed or refractory DLBCL did not include sufficient numbers of patients aged 65 and over to determine whether they respond differently from younger patients.

The effect of end-stage renal disease (CLCR  $< 15$  mL/min) or hemodialysis on XPOVIO pharmacokinetics is unknown.

Please see full Prescribing Information.

To report SUSPECTED ADVERSE REACTIONS, contact Karyopharm Therapeutics Inc. at 1-888-209-9326 or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

## About Karyopharm Therapeutics

Karyopharm Therapeutics Inc. (Nasdaq: KPTI) is an innovation-driven pharmaceutical company dedicated to the discovery, development, and commercialization of novel first-in-class drugs directed against nuclear export and related targets for the treatment of cancer and other major diseases. Karyopharm's Selective Inhibitor of Nuclear Export (SINE) compounds function by binding with and inhibiting the nuclear export protein XPO1 (or CRM1). Karyopharm's lead compound, XPOVIO® (selinexor), received accelerated approval from the U.S. Food and Drug Administration (FDA) in July 2019 in combination with dexamethasone as a treatment for patients with heavily pretreated multiple myeloma. In June 2020, XPOVIO was approved by the FDA as a treatment for patients with relapsed or refractory diffuse large B-cell lymphoma. A Marketing Authorization Application for selinexor for patients with heavily pretreated multiple myeloma is also currently under review by the European Medicines Agency. In addition to single-agent and combination activity against a variety of human cancers, SINE compounds have also shown biological activity in models of neurodegeneration, inflammation, autoimmune disease, certain viruses and wound-healing. Karyopharm has several investigational programs in clinical or preclinical development. For more information, please visit [www.karyopharm.com](http://www.karyopharm.com).

## Forward-Looking Statements

This press release contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Such forward-looking statements include those regarding Karyopharm's beliefs regarding XPOVIO's ability to treat patients with relapsed or refractory diffuse large B-cell lymphoma and expectations related to other XPOVIO regulatory submissions. Such statements are subject to numerous important factors, risks and uncertainties, many of which are beyond Karyopharm's control, that may cause actual events or results to differ materially from Karyopharm's current expectations. For example, there can be no guarantee that any positive developments in the development or commercialization of Karyopharm's drug candidate portfolio will result in stock price appreciation. Management's expectations and, therefore, any forward-looking statements in this press release could also be affected by risks and uncertainties relating to a number of other factors, including the following: the risk that the COVID-19 pandemic could disrupt Karyopharm's business more severely than it currently anticipates, including by reducing sales of XPOVIO, interrupting or delaying research

and development efforts, impacting the ability to procure sufficient supply for the development and commercialization of selinexor or other product candidates, delaying ongoing or planned clinical trials, impeding the execution of business plans, planned regulatory milestones and timelines, or inconveniencing patients; the adoption of XPOVIO in the commercial marketplace, the timing and costs involved in commercializing XPOVIO or any of Karyopharm's drug candidates that receive regulatory approval; the ability to retain regulatory approval of XPOVIO or any of Karyopharm's drug candidates that receive regulatory approval; Karyopharm's results of clinical trials and preclinical studies, including subsequent analysis of existing data and new data received from ongoing and future studies; the content and timing of decisions made by the U.S. Food and Drug Administration and other regulatory authorities, investigational review boards at clinical trial sites and publication review bodies, including with respect to the need for additional clinical studies; the ability of Karyopharm or its third party collaborators or successors in interest to fully perform their respective obligations under the applicable agreement and the potential future financial implications of such agreement; Karyopharm's ability to obtain and maintain requisite regulatory approvals and to enroll patients in its clinical trials; unplanned cash requirements and expenditures; development of drug candidates by Karyopharm's competitors for indications in which Karyopharm is currently developing its drug candidates; and Karyopharm's ability to obtain, maintain and enforce patent and other intellectual property protection for any drug candidates it is developing. These and other risks are described under the caption "Risk Factors" in Karyopharm's Quarterly Report on Form 10-Q for the quarter ended March 31, 2020, which was filed with the Securities and Exchange Commission (SEC) on May 5, 2020, and in other filings that Karyopharm may make with the SEC in the future. Any forward-looking statements contained in this press release speak only as of the date hereof, and, except as required by law, Karyopharm expressly disclaims any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise.

Velcade® is a registered trademark of Takeda Pharmaceutical Company Limited.

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<sup>1</sup> Dr. Leonard has served as a paid consultant to Karyopharm.

Source: Karyopharm Therapeutics Inc.



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